



Prognostic value of the fibrinogen-to-platelet ratio as an inflammatory and coagulative index in patients with gastric cancer

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Abstract

Purpose We assessed the prognostic value of the fibrinogen-to-platelet ratio (FPR) as an inflammatory and coagulative index by examining its clinicopathologic and prognostic efficiency in patients with gastric cancer (GC).

Methods The subjects of this retrospective study were 182 GC patients whose FPR was measured preoperatively between January, 2001 and December, 2006. The FPR was defined as the plasma fibrinogen divided by the platelet counts.

Results Patients aged ≥ 65 years and with venous invasion had a significantly higher FPR ($p=0.02$ and $p<0.01$, respectively) than those aged <65 years and without venous invasion. We found a correlation between the FPR and all recurrences ($p<0.01$). Patients with a low FPR had significantly better overall survival (OS) and relapse-free survival (RFS) rates than patients with a high FPR ($p=0.001$ for both). Furthermore, the FPR was an independent predictor of OS and RFS ($p=0.02$ and 0.001 , respectively), but the fibrinogen level was not. In a subgroup analysis, the FPR was a significant prognostic factor for OS and RFS in patients with pathological stages II/III disease and in patients aged <65 years.

Conclusion The FPR can be calculated easily and is more useful than the fibrinogen level for predicting the prognosis of GC patients. Patients with a high FPR, particularly those with undifferentiated tumors, those with pStage II/III disease, and those aged <65 years, require more intensive chemotherapy.

Keywords Gastric cancer · Fibrinogen-to-platelet ratio · Prognostic index

Introduction

Gastric cancer (GC) is among the most aggressive cancers. In 2015, it was the third leading cause of cancer-related mortality and the fourth most common cancer worldwide [1]. Despite advances in diagnosis and treatment, the prognosis of patients with GC remains poor. In Japan, the current recommended treatment for pathological stage (pStage) II and III GC after curative gastrectomy comprises adjuvant chemotherapy for 12 months with S1 (80 mg/m²) for 4 weeks, followed by 2 weeks of rest [2]; however, the disease course and prognosis of patients with identical cancer staging differ. Therefore, sensitive predictive markers are required to provide personalized treatment.

Many studies have attempted to identify molecular biomarkers that can predict the prognosis of GC patients, and several of these have been evaluated. For example, carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) are used clinically as GC tumor markers during treatment; however, they are not helpful for predicting prognosis [3, 4].

Inflammation and blood coagulation abnormalities, including thrombocytosis and elevated plasma fibrinogen levels are observed in patients with malignant tumors, suggesting that these two parameters reflect the inflammatory and coagulative responses associated with tumor progression. Thrombocytosis [5, 6] and elevated plasma fibrinogen levels [7, 8] have also been associated with the poor prognosis of patients with GC. A previous study found that the formation of platelet–fibrin–tumor cell aggregates are associated with endothelial adhesion and metastatic potential [9]. Based on these findings, we speculated that an index reflecting the binding of fibrinogen to platelets would be more sensitive than either plasma fibrinogen or platelet counts

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individually. Therefore, we assessed the usefulness of the fibrinogen-to-platelet ratio (FPR) to better assess GC prognosis. We collected preoperative FPR data retrospectively from patients who had undergone curative gastrectomy for GC, and evaluated the possible associations among the FPR, clinicopathological factors, and survival.

Methods

Patients

We screened the database of the Nara Medical University for patients with GC and identified 376 patients who had undergone gastrectomy without preoperative treatment, between January, 2001 and December, 2006. All the patients had also undergone esophagogastroduodenoscopy, esophagogram, and abdominal computed tomography to confirm the diagnosis, both clinically and pathologically, before surgery. Clinical and pathological findings, along with clinical stage (cStage) and pStage, were evaluated according to the Japanese classification of gastric carcinoma [10]. Data on preoperative plasma fibrinogen and platelet counts were available for 294 of the 376 patients, and of these, patients with remnant GC, those with synchronous advanced multiple tumors, those with residual tumor(s), those with follow-up of ≤ 12 months, and those with missing data were excluded from the analysis. Finally, the study analyzed data from 182 patients (Fig. 1), 63 of whom with pStage II or III had received adjuvant chemotherapy. Cancer stromal volumes were classified into three categories; namely, scanty stroma (medullary), abundant stroma (scirrhous), and intermediate stroma between the med and sci types (intermediate). The tumor infiltration pattern was also classified into three categories; namely, expanding growth with a distinct border (INFa), infiltrative growth of tumor with no distinct border (INFc), and an intermediate pattern between INFa and INFc (INFb). Although there was no evidence for adjuvant chemotherapy after curative gastrectomy during our study from 2001 to 2006, fluoropyrimidine (S1 or UFT) was given to patients with pStage II or III disease, particularly if it was in pathologically node-positive, as adjuvant chemotherapy in our institution. S1 ($n=22$), UFT ($n=26$), and other agents ($n=16$) were administered for adjuvant chemotherapy.

The institutional review board of the Nara Medical University Hospital approved this study (No. 1372).

Measurements of serum fibrinogen, platelets, and FPR

Serum samples were collected within 1 month before gastrectomy to measure the fibrinogen levels. Assays were performed by medical technicians blinded to the clinical status

of the patient and plasma fibrinogen was measured using an automated coagulation analyzer, the Coapresta 2000 (CP2000, Sekisui Medical, Tokyo, Japan). The manufacturer-recommended normal ranges for plasma fibrinogen concentrations and platelet counts were 200–400 mg/dL and $15.8–34.8 \times 10^4/\mu\text{L}$, respectively. The FPR was calculated as the plasma fibrinogen concentration (A ; mg/dL) divided by the platelet counts ($B \times 10^4/\mu\text{L}$), i.e., $\text{FPR} = A/B$.

Cutoff values of plasma fibrinogen, platelets, and FPR for prognosis

A receiver operating characteristic (ROC) curve was constructed to evaluate the ability of the cutoff values for plasma fibrinogen, platelet counts, and the FPR to predict recurrence. The area under curve (AUC) and its 95% confidence intervals were calculated to derive the optimal cutoff values for predicting recurrence.

Statistical analysis

All statistical analyses were performed using the JMP software program (ver. 11; SAS institute, Cary, NC, USA). Differences in clinicopathological factors were calculated using the Student's t test or Fisher's exact test. Overall survival (OS) and relapse-free survival (RFS) rates were analyzed in patients without cancer at the resection margins and with more than 12 months of follow-up data. OS was defined as the time from the operation until death from any cause. RFS was defined as time from the operation until death or first recurrence. Survival curves were calculated using the Kaplan–Meier method. A p value of less than 0.05 was considered significant. All quantitative data are expressed as mean values \pm the standard deviation.

Results

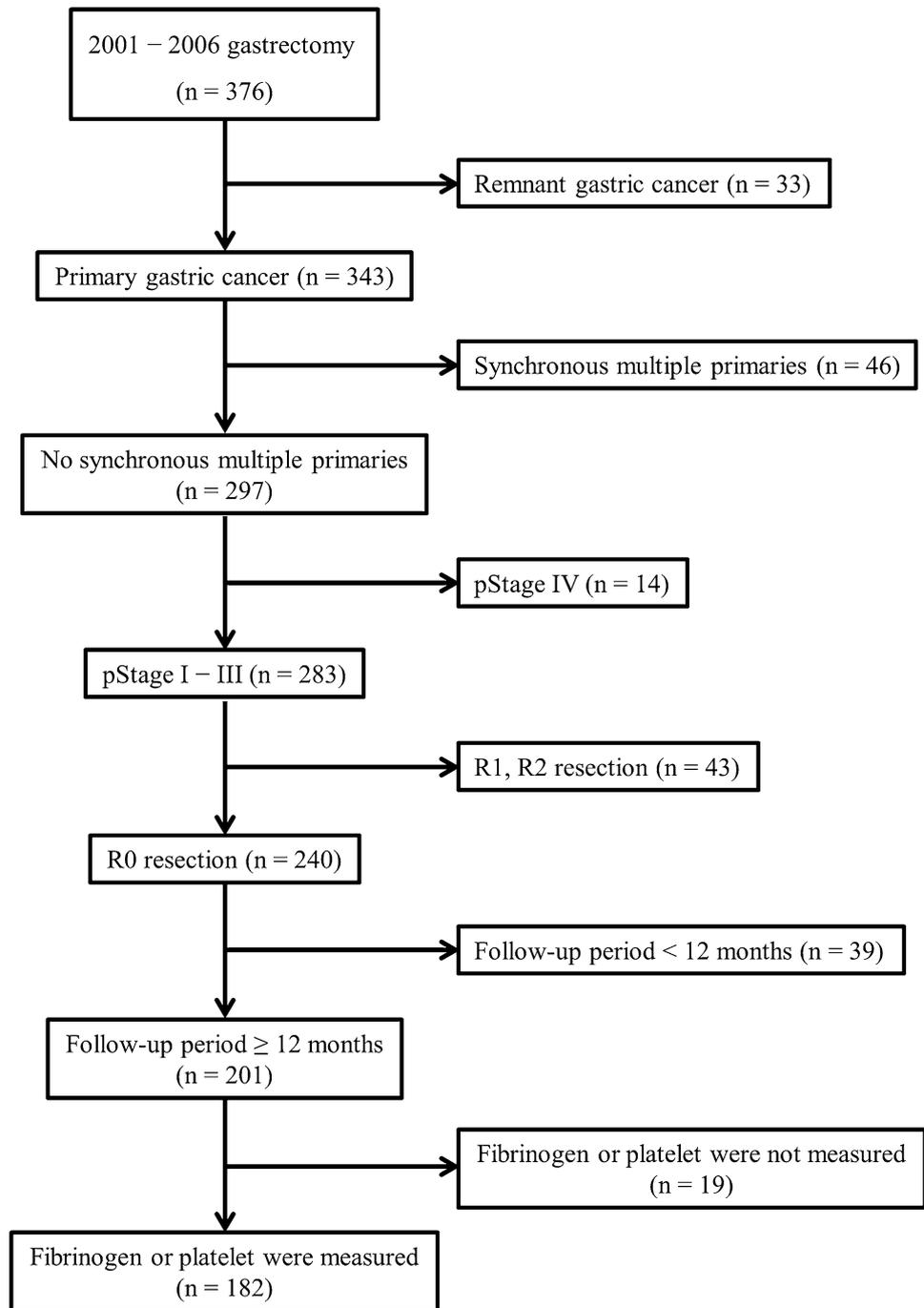
Possible impact of the FPR as an inflammatory and coagulative marker

The FPR is both an inflammatory and a coagulation index. Linear regression analysis revealed a significant association between the FPR and CRP ($r^2=0.06$, $p=0.001$) and between the FPR and D-dimer ($r^2=0.06$, $p=0.005$), respectively.

Clinicopathological factors associated with plasma fibrinogen, platelet counts, and FPR

Table 1 presents the clinicopathological factors associated with plasma fibrinogen, platelet counts, and the FPR. The mean plasma fibrinogen, platelet counts, and FPR were 319.4 ± 88.9 mg/dL, $23.4 \pm 7.6 \times 10^4/\mu\text{L}$, and 14.6 ± 5.5 ,

Fig. 1 Patient flow chart



respectively. Significantly higher plasma fibrinogen levels were found in patients aged ≥ 65 years than in those aged < 65 years, in patients with lymph node metastasis than in those without lymph node metastasis, in patients with cancer tissue stromal volume of “med” or “int” than in those with stromal volume of “sci”, in patients with a tumor infiltration pattern of INFa or INFb than in those with an infiltration pattern of INFc, and in patients with venous invasion than in those without venous invasion ($p < 0.01$ for all). Significantly higher platelet counts were

found in men than in women ($p = 0.02$), in patients with advanced tumors than in those with early-stage tumors ($p < 0.01$), and in patients with lymph node metastasis than in those without lymph node metastasis ($p < 0.01$). A significantly higher FPR was observed in patients aged ≥ 65 years than in those aged < 65 years ($p = 0.02$), and in patients with venous invasion than in those without venous invasion ($p < 0.01$). Taken together, these results revealed that patients with advanced-stage disease tended

Table 1 Clinicopathological factors associated with plasma fibrinogen, platelet counts, and the fibrinogen-to-platelet ratio in patients with gastric cancer ($n = 182$)

Variables	Patients, n	Plasma fibrinogen (mg/dL)		Platelet counts ($\times 10^4 \mu\text{L}$)		FPR	
		Mean (95% CI)	p value	Mean (95% CI)	p value	Mean (95% CI)	p value
		319.4 (306.4–332.4)		23.4 (22.3–24.5)		14.6 (13.8–15.4)	
Gender			0.14		0.02		0.08
Male	137	325.0 (310.0–340.0)		25.8 (23.6–28.0)		15.0 (14.1–15.9)	
Female	45	302.5 (276.4–328.6)		22.6 (21.3–23.9)		13.4 (11.8–15.0)	
Age (years)			< 0.01		0.91		0.02
< 65	96	301.8 (284.2–319.3)		23.5 (21.9–25.0)		13.7 (12.6–14.8)	
≥ 65	86	339.1 (320.5–357.6)		23.3 (21.7–25.0)		15.6 (14.4–16.7)	
Histological classification ^a			0.11		0.41		0.13
Differentiated	90	330.2 (311.8–348.6)		22.9 (21.3–24.5)		15.2 (14.1–16.4)	
Undifferentiated	92	308.9 (290.6–327.1)		23.9 (22.3–25.5)		14.0 (12.9–15.1)	
Depth of tumor invasion (pT) ^a			0.09		< 0.01		0.73
pT1, pT2	97	309.0 (291.2–326.7)		22.4 (20.8–23.9)		14.5 (13.4–15.6)	
pT3, pT4	85	331.3 (312.3–350.2)		24.6 (23.0–26.2)		14.8 (13.6–15.9)	
Lymph node metastasis (pN) ^a			< 0.01		< 0.01		0.45
Negative	104	304.6 (287.7–321.6)		22.0 (20.6–23.5)		14.3 (13.3–15.4)	
Positive	78	339.1 (319.5–358.7)		25.2 (23.6–26.9)		15.0 (13.7–16.2)	
pStage ^a			0.08		0.01		0.85
I	82	308.1 (288.9–327.4)		22.1 (20.5–23.8)		14.4 (13.2–15.6)	
II	47	313.7 (288.3–339.1)		22.8 (20.6–24.9)		14.6 (13.0–16.1)	
III	53	341.8 (317.9–365.8)		26.0 (23.9–28.0)		15.0 (13.5–16.4)	
Cancer stromal volume ^{a,b}			< 0.01		0.09		0.11
Medullary, intermediate type	113	345.0 (329.2–360.8)		24.5 (23.1–26.0)		15.2 (14.1–16.2)	
Scirrhous type	49	278.6 (254.6–302.6)		22.2 (20.0–24.4)		13.6 (12.0–15.2)	
Tumor infiltrative pattern ^{a,c}			< 0.01		0.28		0.06
INFa, INFb	105	339.4 (322.6–356.2)		24.0 (22.5–25.4)		15.3 (14.2–16.4)	
INFc	64	290.2 (268.7–311.8)		22.6 (20.7–24.5)		13.7 (12.3–15.0)	
Lymphatic invasion ^a			0.58		0.22		0.83
Negative	82	315.4 (296.0–334.8)		22.6 (21.0–24.3)		14.5 (13.3–15.7)	
Positive	100	322.7 (305.1–340.2)		24.0 (22.5–25.5)		14.7 (13.6–15.8)	
Venous invasion ^{a,d}			< 0.01		0.1		< 0.01
Negative	158	308.6 (295.3–322.0)		23.0 (21.8–24.2)		14.2 (13.4–15.1)	
Positive	23	392.7 (357.7–427.6)		25.9 (22.7–29.0)		17.4 (13.4–15.1)	
Adjuvant therapy ^c			0.08		< 0.01		0.99
Yes	63	332.2 (311.3–353.1)		25.6 (23.7–27.5)		14.6 (13.2–16.0)	
No	108	309.1 (293.1–325.0)		22.1 (20.7–23.6)		14.6 (13.5–15.6)	
All recurrences			0.06		0.39		< 0.01
Negative	143	312.8 (298.3–327.4)		23.7 (22.4–24.9)		14.6 (13.2–16.0)	
Positive	39	309.1 (315.6–371.4)		22.5 (20.1–24.9)		17.3 (15.6–19.0)	
Lymphatic recurrence			0.07		0.77		< 0.01
Negative	176	317.2 (304.1–330.4)		23.4 (22.2–24.5)		14.4 (13.6–15.2)	
Positive	6	383.3 (312.2–454.6)		24.3 (18.2–30.5)		21.8 (17.5–26.1)	
Hematogenous recurrence			0.99		0.47		0.78
Negative	165	319.4 (305.7–333.1)		23.3 (22.1–24.5)		14.6 (13.8–15.5)	
Positive	17	319.8 (277.1–362.5)		24.7 (21.0–28.4)		14.3 (11.6–16.9)	
Peritoneal recurrence			0.43		0.44		0.1
Negative	157	317.3 (303.3–331.3)		23.6 (22.4–24.8)		14.3 (13.5–15.2)	
Positive	25	332.5 (297.3–367.6)		22.3 (19.3–25.3)		16.3 (14.2–18.4)	

FPR fibrinogen-to-platelet ratio

^aAccording to the Japanese classification of gastric carcinoma

^bA pathological diagnosis was not made in 20 patients

^cA pathological diagnosis was not made in 13 patients

Table 1 (continued)^dA pathological diagnosis was not made in 1 patient^e11 data points were missing

to have high plasma fibrinogen and platelet counts; however, the FPR was not associated with tumor staging.

Next, we investigated the association between plasma fibrinogen, platelet counts, the FPR, and recurrence patterns, but found no correlation between plasma fibrinogen levels and platelet counts or recurrence patterns. Recurrence pattern analysis revealed a significant correlation between the preoperative FPR and all recurrences and lymphatic recurrence in the Student's *t* test (Table 1; $p < 0.01$ for both). However, the number of lymphatic recurrences was small ($n = 6$) in this series. Conversely, the rates of all recurrences and lymphatic, hematogenous, and peritoneal recurrence in the low FPR group were 18.5% (17/92) and 1.1% (1/92), 8.7% (8/92), and 8.7% (8/92), respectively, and those in the high FPR group were 34.4% (31/90) and 5.6% (5/90), and 10.0% (9/90) and 18.9% (17/90), respectively. There was a significant difference between the low and high FPR groups in the rates of all recurrences and peritoneal recurrence ($p < 0.01$ and $p = 0.04$, respectively) in Fisher's exact test.

FPR as an independent risk factor of overall survival and relapse-free survival

The cutoff values of plasma fibrinogen and the FPR that can predict prognosis were defined as 260 mg/dL (AUC 0.59; $p = 0.01$) and 13.5 (AUC 0.63; $p = 0.01$), respectively, while no predictive cutoff value for platelet counts was obtained. The cutoff value for the platelet counts was defined as $23 \times 10^4/\mu\text{L}$, using the mean approximate value. Based on OS and RFS rates, patients with low FPR values had significantly better survival rates than those with high FPR values ($p = 0.001$ and $p < 0.001$, respectively; Fig. 2a, b). Moreover, according to the FPR, this result tended to be independent of cancer stage in OS and RFS ($p = 0.11$ and $p = 0.06$, respectively, in pStage I; $p = 0.007$ and $p = 0.006$, respectively, for pStage II and III disease; Fig. 2c–f). Table 2 summarized the univariate analysis results, which identified tumor depth, lymph node metastasis, lymphatic invasion, venous invasion, plasma fibrinogen, and the FPR as risk factors for OS and RFS. Multivariate analysis revealed that the FPR was an independent risk factor for OS and RFS, along with tumor depth and lymph node metastasis status ($p = 0.02$ and $p = 0.001$, respectively).

Subgroup analysis of FPR for GC prognosis

The FPR was helpful for predicting the OS of men (HR 0.48; 95% CI 0.23–0.91), in patients aged < 65 years (HR 0.34;

95% CI 0.14–0.78), patients with undifferentiated tumors (HR 0.23; 95% CI 0.09–0.53), patients with pT2/3 (HR 0.49; 95% CI 0.25–0.95), and patients with pStage II and III disease (HR 0.45; 95% CI 0.23–0.85) (Fig. 3). Moreover, it was helpful for predicting the RFS of men (HR 0.44; 95% CI 0.22–0.84), patients aged < 65 years (HR 0.30; 95% CI 0.13–0.66), patients with undifferentiated tumors (HR 0.21; 95% CI 0.08–0.48), and patients with pStage II and III disease (HR 0.44; 95% CI 0.23–0.83) (Fig. 3).

Discussion

The aim of this study was to identify a sensitive and easily calculable prognostic index for GC. We focused on an inflammatory and coagulation index because it is well known that abnormalities in inflammation and coagulation, including thrombocytosis and elevated fibrinogen, are associated with malignant tumors. Platelets and fibrinogen influence tumor biology through several possible mechanisms [11] and fibrinogen and platelets collectively play a crucial role in tumor growth, invasion, and metastasis [12–14]. Specifically, the potential benefits for tumor growth and metastasis include the local release of platelet-derived growth factors, while other effectors can promote tumor cell growth and stroma formation. For example, local platelet–fibrin deposition may sustain tumor cell immobilization within the circulation and provide a supportive matrix for cell proliferation, and platelets associated with the embolic tumor cells may limit antitumor cell immune surveillance mechanisms [11]. Moreover, the formation of platelet–fibrin–tumor cell aggregates may be associated with endothelial adhesion and metastatic potential [9]. Thus, we speculated that the FPR reflects the possibility of fibrinogen binding to platelets, and that it could predict prognosis better than either plasma fibrinogen levels or the platelet count. We investigated the FPR as an index that can reflect the clinicopathological characteristics and act as a prognostic index for GC.

First, we found that the FPR correlates significantly with the D-dimer value, which is a well-known marker of coagulation and used routinely in the diagnosis of venous thromboembolism. Therefore, we suggest that the FPR reflects the status of platelet–fibrin aggregates, which are the cause of thrombus formation and are associated with cancer progression.

Second, in terms of the clinicopathological impact of plasma fibrinogen, platelet counts, and the FPR, we found that elevated plasma fibrinogen and platelet counts are

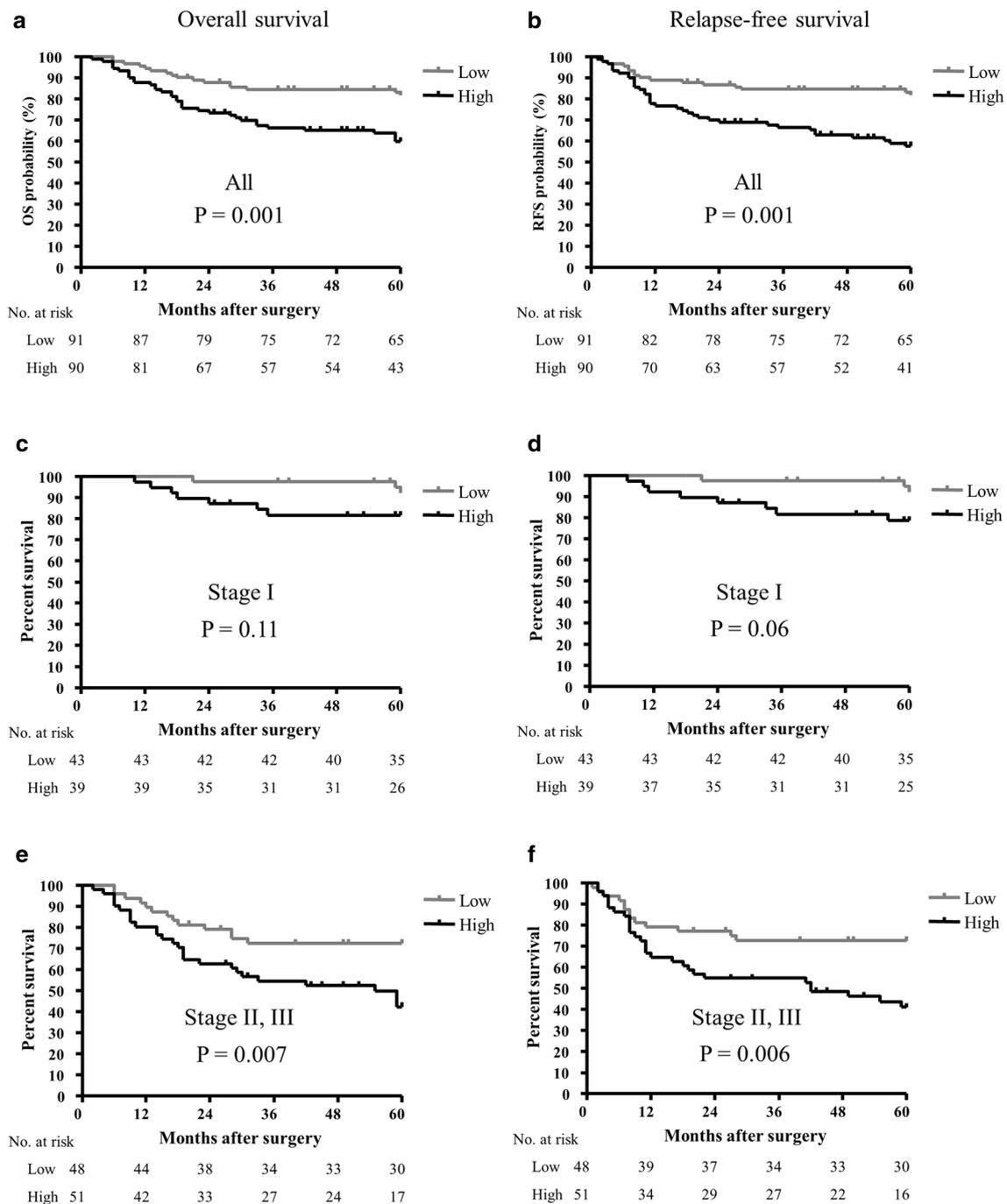


Fig. 2 Survival analysis. **a** Overall survival (OS) in fibrinogen-to-platelet ratio (FPR) status at all stages ($p=0.001$). **b** Relapse-free survival (RFS) in FPR status at all stages ($p=0.001$). **c** OS in FPR status

at pStage I ($p=0.11$). **d** RFS in FPR status at pStage I ($p=0.06$). **e** OS in FPR status at pStage II and III ($p=0.007$). **f** RFS in FPR status at pStage II and III ($p=0.006$)

associated with the advanced tumor status; however, the FPR was independent of tumor depth and lymph node metastasis. Previous studies have reported that plasma fibrinogen is associated with age, tumor size, tumor depth, lymph node metastasis, liver metastasis, and tumor stage [7, 15], and that platelet counts are associated with age, tumor size, tumor

invasion, lymph node metastasis, distant metastasis, and TNM stage [16]. Our results concur with these reports. We also found that the FPR is associated with all forms of recurrence after curative gastrectomy. Although analysis of recurrence patterns showed no association between the FPR and lymphatic invasion, the FPR was associated with lymphatic

Table 2 Independent risk factors for patient survival

Variables	Univariate analysis			Multivariate analysis		
	Crude HR	95% CI	<i>p</i> value	Adjusted HR	95% CI	<i>p</i> value
Overall survival						
Gender (female)	0.69	0.33–1.32	0.28			
Age (≥ 65 years)	1.47	0.85–2.56	0.17			
Histological classification ^a (undifferentiated)	0.98	0.57–1.71	0.96			
Depth of tumor invasion ^a (pT3, pT4)	4.39	2.41–8.57	<0.001	2.11	1.04–4.51	0.04
Lymph node metastasis ^a (positive)	4.81	2.67–9.20	<0.001	2.48	1.23–5.25	0.01
Cancer stromal volume ^a (scirrhous type)	1.45	0.80–2.59	0.21			
Tumor infiltrative pattern ^a (INFc)	1.33	0.75–2.32	0.32			
Lymphatic invasion ^a (positive)	2.88	1.58–5.61	<0.001	1.86	0.98–3.73	0.06
Venous invasion ^a (positive)	3.26	1.67–5.97	0.001	1.38	0.68–2.64	0.36
Plasma fibrinogen (≥ 260 mg/dL)	2.04	1.16–3.68	0.002	1.78	0.76–4.69	0.19
Platelet counts ($\geq 23 \times 10^4 \mu\text{L}$)	1.13	0.66–1.96	0.64			
FPR (≥ 13.5)	2.38	1.35–4.35	0.001	2.05	1.10–4.02	0.02
Relapse-free survival						
Gender (female)	0.66	0.32–1.26	0.22			
Age (≥ 65 years)	1.34	0.78–2.30	0.29			
Histological classification ^a (undifferentiated)	1.04	0.61–1.79	0.87			
Depth of tumor invasion ^a (pT3, pT4)	5.39	3.14–9.44	<0.001	2.13	1.06–4.43	0.03
Lymph node metastasis ^a (positive)	4.37	2.48–8.06	<0.001	2.28	1.16–4.66	0.02
Cancer stromal volume ^a (scirrhous type)	1.49	0.83–2.61	0.18			
Tumor infiltrative pattern ^a (INFc)	1.34	0.77–2.31	0.3			
Lymphatic invasion ^a (positive)	2.83	1.58–5.39	<0.001	1.92	1.04–3.76	0.04
Venous invasion ^a (positive)	3.67	1.92–6.62	<0.001	1.64	0.83–3.09	0.15
Plasma fibrinogen (≥ 260 mg/dL)	1.91	1.12–3.32	0.002	1.54	0.68–3.84	0.31
Platelet counts ($\geq 23 \times 10^4 \mu\text{L}$)	1.13	0.66–1.93	0.66			
FPR (≥ 13.5)	2.5	1.43–4.56	0.001	2.28	1.22–4.47	0.001

FPR fibrinogen-to-platelet ratio

^aPathological classification in the Japanese classification of gastric carcinoma

recurrence, which could be attributed to the small number of cases with lymphatic recurrence in this series ($n = 6$). Furthermore, while the FPR was associated with venous invasion, it was not associated with hematogenous recurrence, probably because we excluded patients with hematogenous metastasis at the time of surgery, from the analysis. Thus, the association between the FPR and hematogenous metastasis is unclear from our results. Although we showed that the FPR is significantly correlated with total recurrence; our results do not support an association between the FPR and recurrence patterns.

Finally, we found that the FPR is an independent risk factor for OS and RFS, as well as tumor depth and lymph node metastasis. High plasma fibrinogen levels were associated with poor prognosis in the univariate analysis, but plasma fibrinogen was not an independent prognostic factor for GC in the multivariate analysis. This may be because the elevated plasma fibrinogen levels were associated with an advanced tumor status. The FPR values were independent

of tumor status and stages, and therefore, may be more useful as an independent prognostic predictor than plasma fibrinogen levels for GC. Our subgroup analysis revealed that the FPR could be a useful prognostic index for male patients, aged < 65 years, with undifferentiated tumors, or with pStages II/III disease. Furthermore, no presumable difference in the prognostic value was observed between high and low FPRs in elderly patients because they have higher plasma fibrinogen levels than younger patients. Our results suggest that intensive chemotherapeutic regimens such as neoadjuvant chemotherapy or doublet adjuvant chemotherapy should be considered for patients aged < 65 years, with undifferentiated tumors, or advanced stages disease with a high preoperative FPR. Many molecular biomarkers have been explored to predict the prognosis of patients with GC; however, we require reliable indices that can select patients with a poor prognosis for locally advanced GC because they require potent chemotherapy. Some studies on GC have reported that elevated fibrinogen levels are associated with

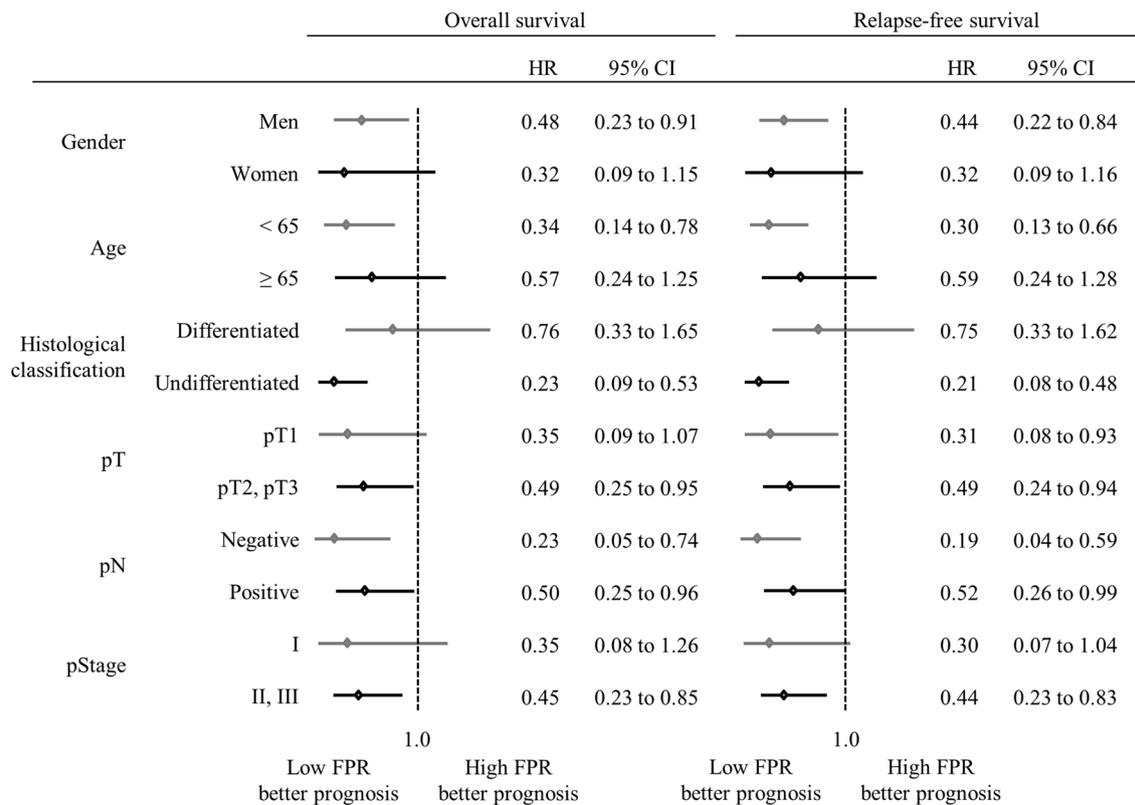


Fig. 3 Subgroup analysis. OS and RFS according to FPR status were analyzed in groups based on gender, age, histological classification, pT, pN, and pStage

poor clinical outcomes [7, 8, 15, 17–19], and that patients with thrombocytosis have a poor prognosis [5, 16, 20, 21]. The present study found that the FPR is more important than either plasma fibrinogen levels or platelet counts. In contrast, other studies have reported prognostic indices based on coagulation and inflammation in GC, such as the neutrophil-lymphocyte ratio (NLR), and the platelet-lymphocyte ratio (PLR) [22, 23]; however, both the NLR and PLR could predict survival only in early GC, and the NLR was a better predictor of OS than PLR [23]. Moreover, as the NLR could predict survival in stages I, II, and IV [22], the use of specific indices for GC prognosis remains controversial and insufficient. Some studies have shown that the AUCs of the NLR were 0.52 [15], 0.58 [24], and 0.55 [23], and that the AUC of the PLR was 0.57 [7, 15]. Our study showed that the AUC of FPR (0.63) was better than other indices, but more data from a nationwide clinical database are required to validate our results.

The present study had several limitations. First, it was a retrospective study with data from a single institution and our study period was 2001–2006s, the sample size was small and we were unable to measure preoperative plasma fibrinogen levels and platelet counts in some patients. Further studies are needed to validate the accuracy of the FPR cutoff

values and their prognostic efficacy, either prospectively or retrospectively and with a larger sample size.

In conclusion, the preoperative FPR can be calculated easily and is more useful than the plasma fibrinogen level to predict the prognosis for GC patients. Patients with a high preoperative FPR, particularly those with undifferentiated tumors, pStage II/III disease, or aged < 65 years require more intensive chemotherapy such as neoadjuvant chemotherapy or doublet adjuvant chemotherapy.

Compliance with ethical standards

Conflict of interest We have no conflicts of interest to declare in association with the present study.

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